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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/934,680	08/23/2001	Duncan W. McBranch	8971-017-27	8385

7590 11/05/2003

Supervisor, Patent Prosecution Services  
PIPER MARBURY RUDNICK & WOLFE LLP  
1200 Nineteenth Street, N.W.  
Washington, DC 20036-2412

EXAMINER
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LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/934,680

Applicant(s)

MCBRANCH ET AL.

Examiner

Frank W Lu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08 August 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 14-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 8/23/2001 (original) is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3/2003 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election with traverse of Group I, claims 1-13 filed on August 8, 2003 is acknowledged. The traversal is on the ground(s) that "[T]he basis for Applicants traversal is that there is no undue burden on the Examiner. The Examiner has argued that the product of Group I can be used in the processes of Group II and Group III. All of the claims of the present application are therefore searchable in closely related art classifications and, as such, overlapping areas of search for the different Groups designated by the Restriction Requirement are likely. Reconsideration of the Restriction Requirement is respectfully requested".

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the restriction requirement nor persuasive toward the relaxation of same such that Groups I, II, and III will be examined. First, although the examiner agrees that some searches from Groups I, II, and III may overlap, since Groups II and III are directed to method and have method steps that are not required for Group I, there is an undue search burden on the examiner. Second, since Groups II and III are dependent on Group I, the examiner agrees to rejoin product dependent claims 14-21 (Groups II and III) into product claims 1-13 after product claims 1-13 reach an allowable state.

Therefore, the requirement is still deemed proper and is therefore made FINAL and claims 1-13 will be examined.

***Claim Objections***

2. Claim 11 is objected to because of the following informality: “said fluorescence dye” should be “said fluorescent polymer” in order to correspond to claims 1-10, 12, and 13.
3. Claim 13 is objected to because of the following informality: there should be a coma after the phrase “porous beads”.

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:  
  
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
5. Claims 1-13 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
6. Claim 1 is rejected as vague and indefinite in view of the phrase “said recognition element being further bound together by a second tethering element to a property altering element which alters fluorescence emitted by said fluorescent polymer when complexed together to a distinguishable degree” because it is unclear what are complexed together. Does a complex recited in claim 1 have a target nucleic acid? Please clarify.
7. Claim 3 recites the limitation “said sequence of peptide nucleic acids” in the claim. There is insufficient antecedent basis for this limitation in the claim since there is no “peptide

nucleic acids” in claim 1. In view of claims 1 and 2, claim 3 appears to be dependent on claim

2. Please clarify.

***Claim Rejections - 35 USC § 102***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1-7, 12, and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Coull *et al.*, (US Patent No. 6,355,421, filed on October 27, 1998).

The rejection is based on that the left arm segment labeled with the fluorophore (see Figure 11, below) is a fluorescent polymer.

Coull *et al.*, teach methods, kits, and compositions pertaining to PNA molecular beacons.

Regarding claims 1-3, as shown in Figure 11, Coull *et al.*, teach configuration III of a PNA molecular beacon which comprises two arm segments, two flexible linkers (L1 and L2), one probing segment, one fluorophore (1) and one quencher (2). Since the left arm segment comprising 2-5 PNA units (see column 16, last paragraph) is labeled with a fluorophore and it is known that the left arm segment comprising 2-5 PNA units is a polymer, the left arm segment labeled with the fluorophore is a fluorescent polymer as recited in claim 1. Since the left arm segment and the probe segment are connected by L1 and the probe segment can bind to a target nucleic acid, Coull *et al.*, disclose a fluorescent polymer bound together by a first tethering

element to a recognition element which binds to a target nucleic wherein L1 and the probe segment are first tethering element and a recognition element respectively as recited in claim 1. Since the right arm segment labeled with the quencher and the probe segment are connected by L2 and, after hybridization of the PNA molecular beacon to a target nucleic acid, the fluorescence of the left arm segment is altered due to fluorescence energy transfer between the donor (ie., the fluorophore) and acceptor (ie., the quencher) (see columns 12 and 13), L2 plus the right arm segment together and the quencher is a second tethering element and a property altering element respectively as recited in claim 1 and Coull *et al.*, disclose that, in the presence of binding of said recognition element to said target nucleic acid, the fluorescence emitted by said fluorescent polymer (ie., the left arm segment labeled with the fluorophore) is altered from that emitted when said binding between said recognition element (ie., the probe segment) and said target nucleic acid does not occur as recited in claim 1. Since the probe segment comprises 5-30 PNA subunits and can hybridize with a single stranded target nucleic acid (see column 16, lines 17-35), claims 2 and 3 are anticipated by Coull *et al.*. Since the quencher can be a fluorescence dye (see column 12, lines 49-59), claim 4 is anticipated by Coull *et al.*

Regarding claim 5, since L1 or L2 can be  $-C(S)(CW_2)_p-$  wherein W is H, p is 0-10 (see column 15, second and third paragraphs) and S is with two negative charges, Coull *et al.*, disclose a divalent chemical moiety (ie., S with two negative charges) of up to 10 carbon atoms in length as recited in claim 5

Regarding claims 6 and 7, since Coull *et al.*, teach that the left arm segment labeled with the fluorophore comprises 2-5 PNA units with a formula in column 11 and the atoms in this formula conjugate each other and form a backbone, claim 6 is anticipated by Coull *et al.*. Since

the left arm segment labeled with the fluorophore comprises 2-5 PNA units is neutral if PNA units and the fluorophore do not carry any charge, the left arm segment labeled with the fluorophore is a neutral polymer as recited in claim 7.

Regarding claims 12 and 13, since Coull *et al.*, teach that a PNA molecule beacon is immobilized on a surface selected from membrane, glass, controlled pore glass, polystyrene particle (bead), silica, and gold nanoparticle (see columns 20 and 21) and the left arm segment labeled with the fluorophore (ie., the fluorescent polymer) is part of the PNA molecule beacon taught by Coull *et al.*, Coull *et al.*, disclose that said fluorescent polymer is affixed to a support as recited in claims 12 and 13.

Therefore, Coull *et al.*, teach all limitations recited in claims 1-7, 12, and 13.

10. Claims 1-7, 12, and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Coull *et al.*, (October 27, 1998).

The rejection is based on that the fluorophore that labels the left arm segment (see Figure 11, below) is a fluorescent polymer.

Coull *et al.*, teach methods, kits, and compositions pertaining to PNA molecular beacons.

Regarding claims 1-3, as shown in Figure 11, Coull *et al.*, teach configuration III of a PNA molecular beacon which comprises two arm segments, two flexible linkers (L1 and L2), one probing segment, one fluorophore (1) and one quencher (2). Since the left arm segment is labeled with a fluorophore such as Cy3 (see column 12, lines 49-59) and it is known that Cy3 has five  $-CH_2-$  (see attachment for Cy 3 NHS ester) the fluorophore such as cy3 is a fluorescent polymer containing multiple  $-CH_2-$  as recited in claim 1. Since the left arm segment labeled

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with the fluorophore such as Cy3 and the probe segment are connected by L1 and the probe segment can bind to a target nucleic acid, Coull *et al.*, disclose a fluorescent polymer bound together by a first tethering element to a recognition element which binds to a target nucleic wherein the left arm segment plus L1 together and the probe segment are first tethering element and a recognition element respectively as recited in claim 1. Since the right arm segment labeled with the quencher and the probe segment are connected by L2, and, after hybridization of the PNA molecular beacon to a target nucleic acid, the fluorescence of the left arm segment is altered due to fluorescence energy transfer between the donor (ie., the fluorophore) and acceptor (ie., the quencher) (see columns 12 and 13), L2 plus the right arm segment together and the quencher are a second tethering element and a property altering element respectively as recited in claim 1 and Coull *et al.*, disclose that in the presence of binding of said recognition element to said target nucleic acid, the fluorescence emitted by said fluorescent polymer (ie., the fluorophore that labels the left arm segment) is altered from that emitted when said binding between said recognition element (ie., the probe segment) and said target nucleic acid does not occur as recited in claim 1. Since the probe segment comprises 5-30 PNA subunits and can hybridize with a single stranded target nucleic acid (see column 16, lines 17-35), claims 2 and 3 are anticipated by Coull *et al.*. Since the quencher can be a fluorescence dye (see column 12, lines 49-59), claim 4 is anticipated by Coull *et al.*.

Regarding claim 5, since L1 or L2 can be  $-C(S)(CW_2)_p-$  wherein W is H, p is 0-10 (see column 15, second and third paragraphs) and S is with two negative charges, Coull *et al.*, disclose a divalent chemical moiety (ie., S with two negative charges) of up to 10 carbon atoms in length as recited in claim 5



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Regarding claims 6 and 7, since Cy3 (ie., the fluorophore polymer) is a conjugated compound with repeat  $-CH_2-$  units, claim 6 is anticipated by Coull *et al.*. Since claim 7 only requires that fluorescent polymer is neutral or anionic or cationic, Cy3 taught by Coull *et al.*, is the fluorescence polymer recited in claim 7.

Regarding claims 12 and 13, since Coull *et al.*, teach that a PNA molecule beacon is immobilized on a surface selected from membrane, glass, controlled pore glass, polystyrene particle (bead), silica, and gold nanoparticle (see columns 20 and 21), the PNA molecule beacon taught by Coull *et al.*, is labeled with the fluorescent polymer, Coull *et al.*, disclose that said fluorescent polymer is directly affixed to a support as recited in claims 12 and 13.

Therefore, Coull *et al.*, teach all limitations recited in claims 1-7, 12, and 13.

### ***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coull *et al.*, (October 27, 1998) as applied to claims 1-7, 12, and 13 above (based on the rejection made in item 10), and further in view of Chen *et al.*, (PNAS, 96, 12287-12292, October 1999).

The teachings of Coull *et al.*, have been summarized previously, *supra*.

Coull *et al.*, do not disclose that said fluorescent polymer comprises repeat units each containing a fluorescent dye pendant on a backbone moiety as recited in claim 8 wherein the number of repeat units is greater than or equal to 33 as recited in claim 9 and said fluorescent polymer is a J-aggregate as recited in claim 10 or is a negatively charged dye chromophore as recited in claim 11.

Chen *et al.*, teach highly sensitive biological and chemical sensors based on reversible fluorescence quenching in a conjugated polymer. One of fluorescent polyanionic conjugated polymers, MPS-PPV, comprised about 1000 monomer repeat units and the use of this fluorescence polymer led to a greater than million-fold amplification of the sensitivity to fluorescence quenching relative to that of corresponding small conjugated molecules with similar structure (see page 12287).

Regarding claims 8-11, since MPS-PPV is a fluorescent polyanionic conjugated polymer comprising about 1000 phenylene vinylene (PPV) (see page 12287), Chen *et al.*, disclose that a fluorescent polymer comprises repeat units each containing a fluorescent dye pendant on a backbone moiety as recited in claim 8 wherein the number of repeat units is greater than 33 as recited in claim 9. Since MPS-PPV becomes an aggregate in the presence of divalent cations

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(see page 12289, right column) and the specification describes that J-aggregation is one of non-covalent interactions (see the specification, page 5, lines 6-14), MPS-PPV is a fluorescent polymer that can form a J-aggregation as recited in claim 10. Since MPS-PPV is a fluorescent polyanionic conjugated polymer, MPS-PPV is a negatively charged dye chromophore as recited in claim 11.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a chemical moiety comprising a fluorescent polymer as recited in claims 8-11 in view of the prior art of Coull *et al.*, and Chen *et al.*. One having ordinary skill in the art would have been motivated to do so because the use of the fluorescence polymer taught by Chen *et al.*, would lead to a greater than million-fold amplification of the sensitivity to fluorescence quenching relative to that of corresponding small conjugated molecules with similar structure (see Chen *et al.*, page 12287). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to make a chemical moiety comprising a fluorescent polymer as recited in claims 8-11 since Chen *et al.*, have successfully made or used a fluorescent polymer as recited in claims 8-11.

### *Conclusion*

13. No claim is allowed.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official

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Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.



Frank Lu  
PSA  
October 31, 2003

*attachment for the office action*

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Cy3B NHS Ester

Cy3.5 NHS Ester

Cy5 NHS Ester

Cy5 Maleimide and Hydrazide

Cy5Q NHS Ester

Cy5.5 NHS Ester

Cy7 NHS Ester

Cy7Q NHS Ester

Dye Protein Ratio Calculator

Effects of Conjugation

Labeling Information

Signal Stability

Environmental Effects - DMSO

Environmental Effects - pH

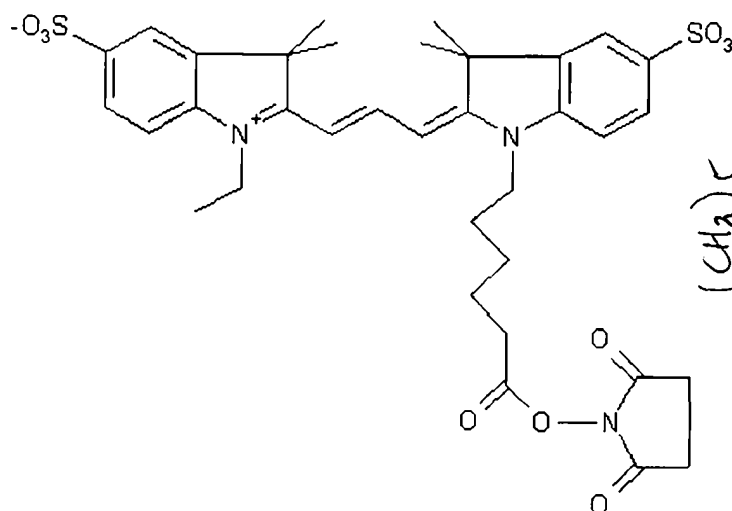
Energy Transfer

Publications

FRET Labelling Fluor Codes

Generic Labelling Fluor Codes

What's New

**Cy3 NHS Ester****Structure**To view the Cy3 NHS structure in 3D, [click here](#)For this you will need the [Chime](#) web browser plugin.**MW = 765.95**

Structure shown as mono-functional NHS ester.

**Spectra**